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Novartis marks World CML Day with update on global research program to evaluate whether Ph+ CML patients can live treatment-free

- *CML community recognizes September 22 as World CML Day to raise awareness of the needs of patients living with CML*
- *Novartis commemorates World CML Day, announcing 100+ study sites across 40 countries now enrolling patients to its global treatment-free remission clinical trials*
- *Treatment-free remission program evaluates whether patients can maintain undetectable levels of disease after stopping nilotinib therapy*

Basel, September 19, 2013 – Novartis commemorates World CML Day by announcing the latest milestone in its unique clinical trial program evaluating the potential for patients with Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) to maintain undetectable levels of disease after stopping drug therapy — a concept called treatment-free remission. More than 100 study sites are now enrolling patients to the trial program.

Since 2008, organizations around the world have recognized World CML Day[1]. The date, September 22 or 9/22, was symbolically chosen to represent the genetic material that is associated with CML — the missing section from chromosome 22 shifts to chromosome 9 and vice versa, in a phenomenon called "translocation[2]." Known as the Philadelphia chromosome, this genetic mutation is present in about 95% of CML patients[3].

"As a leader in CML, Novartis is proud to support World CML Day through our continued dedication to ongoing research in this disease," said Hervé Hoppenot, President, Novartis Oncology. "Given that nilotinib has been shown in large clinical trials to drive deeper levels of responses in more than twice as many patients as imatinib, we are now looking to the next phase and exploring if nilotinib can treat the disease to a point where drug therapy is no longer needed, representing the next step in what may be possible for patients living with Ph+ CML."

Over the past decades, Novartis research in Ph+ CML has helped transform the disease from a fatal diagnosis to a chronic condition for many patients. Today, the company continues its long-standing commitment to the global CML community. The Novartis treatment-free remission clinical trial program* includes eight studies that are now underway and actively enrolling Ph+ CML patients in more than 100 global sites across 40 countries[4]. In total, it is planned that more than 2,500 patients will be enrolled in these

* In the Novartis treatment-free remission clinical trial program, molecular response (reduction of BCR-ABL transcripts in the blood of patients) is measured at four levels, based on an international standard:

- MMR (≤ 0.1% BCR-ABL)
- MR4 (≤ 0.01% BCR-ABL)
- MR4.5 (≤ 0.0032% BCR-ABL)
- Undetectable BCR-ABL (no detectable BCR-ABL transcript level with sample sensitivity of at least 4.5 log)

studies and an estimated nearly 1,000 patients will aim to stop treatment as part of these studies[4].

Globally, Novartis is sponsoring four treatment-free remission studies, including:

- ENESTfreedom[5] – a Phase II study in Ph+ CML patients in chronic phase who achieved and maintained MR4.5 on nilotinib as first-line treatment. More information, including addresses and contact information for each study site, can be found on www.clinicaltrials.gov, identifier # NCT01784068.
- ENESTop[6] – a Phase II study in Ph+ CML patients in chronic phase who have achieved and maintained MR4.5 on nilotinib after switching from imatinib. More information, including addresses and contact information for each study site, can be found on www.clinicaltrials.gov, identifier # NCT01698905.
- ENESTpath[7] – a Phase III study in Ph+ CML patients in chronic phase who have switched to nilotinib from imatinib and have achieved and maintained MR4.0. More information, including addresses and contact information for each study site, can be found on www.clinicaltrials.gov, identifier # NCT01743989.
- ENESTgoal[8] – a Phase II study in Ph+ CML patients in chronic phase who have achieved and maintained MR4.5 on nilotinib after switching from imatinib. More information, including addresses and contact information for each study site, can be found on www.clinicaltrials.gov, identifier # NCT01744665.

Novartis is also providing support for four investigator-initiated studies (STAT-2, NILst, CML V, NILO POST-STIM)[4]. These studies are led by independent investigators in sites in Japan, Germany and France.

Stopping treatment is not a clinical recommendation and should only be attempted in the context of a well conducted clinical study. A very important part of these treatment-free remission studies is the inclusion of regular molecular monitoring with International Scale Real-Time Quantitative Polymerase Chain Reaction (IS RT-Q-PCR) testing. Once treatment is stopped molecular monitoring is used to identify if a patient's level of disease remains in deep molecular response or if the reintroduction of treatment is needed[5-8].

ENESTfreedom study details[5]

ENESTfreedom is a Phase II, single-arm, open-label study to determine if adults with Ph+ CML can live without drug therapy after stopping treatment with nilotinib. Eligible patients must have maintained MR4.5 with nilotinib treatment in the first-line setting for at least two years before entering the study. Following a one-year consolidation phase, patients who continue to sustain MR4.5 will enter the treatment-free phase. Patients will be monitored closely with regular IS RT-Q-PCR testing.

The primary endpoint is the percentage of patients who are in major molecular response (MMR) at 48 weeks after starting the treatment-free phase and no restarting of nilotinib treatment.

ENESTop study details[6]

ENESTop is a Phase II, single-arm, open-label study designed to determine if adults with Ph+ CML can live without drug therapy after stopping treatment with nilotinib. Eligible patients have been on treatment with nilotinib for at least two years (with the combined time on imatinib and nilotinib for at least three years) and have maintained MR4.5 for at least one year before entering the treatment-free phase. Patients will be monitored closely with regular IS RT-Q-PCR testing.

The primary endpoint is the proportion of patients in treatment-free remission and no loss of MMR or MR4 within the first 12 months of nilotinib cessation.

ENESTpath study details[7]
ENESTpath is a prospective, randomized, open-label, two arm Phase III study designed to evaluate the rate of treatment-free remission in Ph+ CML patients at 12 months after two different durations of consolidation treatment with nilotinib. Eligible patients must have been treated with imatinib for a minimum of two years, being at least in complete cytogenetic response, but have not achieved MR4.0 at study start. Patients entering the study will have two years of nilotinib treatment. If sustained MR4.0 is achieved during the second year of nilotinib treatment, patients will be eligible to be randomized to either enter the treatment-free remission phase immediately, or continue for another year of consolidation with nilotinib treatment and, if still in sustained MR4.0, enter the treatment-free remission phase. Patients will be monitored closely with regular IS RT-Q-PCR testing.

The primary endpoint is the proportion of patients who remain in treatment-free remission (≥ MR4.0) without molecular relapse at the end of 12 months in the treatment-free remission phase of the study. This study compares the nilotinib 12-month consolidation treatment arm (arm 1) with the nilotinib 24-month consolidation treatment arm (arm 2) to determine the optimal duration of the consolidation phase.

ENESTgoal study details[8]
ENESTgoal is a US-only Phase II randomized, open-label, two arm, multicenter study designed to determine if adults with Ph+ CML can live without drug therapy after stopping treatment with nilotinib. Eligible patients must have been on treatment with imatinib for at least one year and have achieved a BCR-ABL level of less than or equal to MMR and greater than MR4.5 as measured by IS RT-Q-PCR testing. Patients will switch to nilotinib once entering the study and will have three years of treatment. If MR4.5 is achieved during the third year of treatment, patients will be eligible to be randomized to either enter the treatment-free remission phase immediately, or continue receiving nilotinib for another year before being eligible to enter the treatment-free phase. Patients will be monitored closely with regular IS RT-Q-PCR testing.

The primary endpoint is the percentage of patients remaining in the remission phase (no confirmed loss of MR4.0 and no restarting of treatment with nilotinib) at six months from the start of treatment-free phase, with no confirmed loss of MR4.0 and no restarting of treatment with nilotinib.

About Tasigna (nilotinib)
Tasigna® (nilotinib) is approved in more than 90 countries for the treatment of chronic phase and accelerated phase Philadelphia chromosome-positive chronic myelogenous leukemia (Ph+ CML) in adult patients resistant or intolerant to at least one prior therapy, including Glivec†, and for the treatment of adult patients with newly diagnosed Ph+ CML in chronic phase. Take twice daily 12 hours apart. Do not take with food. No food to be consumed for 2 hours before or one hour after dosing. Avoid grapefruit juice and CYP3A4 inhibitors.

Tasigna Important Safety Information
Use with caution in patients with uncontrolled or significant cardiac disease and in patients who have or may develop prolongation of QTc. Low levels of potassium or magnesium must be corrected prior to Tasigna administration. Monitor closely for an effect on the QTc interval. Baseline ECG is recommended prior to initiating therapy and as clinically indicated. Uncommon cases (0.1 to 1%) of sudden death have been reported in clinical studies in patients with significant risk factors.

Use with caution in patients with liver impairment, with a history of pancreatitis and with total gastrectomy. Patients with rare hereditary problems of galactose intolerance, severe

† Known as Gleevec® (imatinib mesylate) tablets in the US, Canada and Israel.

lactase deficiency or glucose-galactose malabsorption should not use Tasigna. Tasigna may cause fetal harm in pregnant women. Women taking Tasigna should not breastfeed.

The most frequent Grade 3 or 4 adverse events are hematological (neutropenia and thrombocytopenia) which are generally reversible and usually managed by withholding Tasigna temporarily or dose reduction. Monitor blood counts regularly. Pancreatitis has been reported. The most frequent non-hematologic adverse events were rash, pruritus, nausea, fatigue, headache, alopecia, myalgia, constipation and diarrhea. Most of these adverse events were mild to moderate in severity.

Please see full Prescribing Information available at www.tasigna.com.

About Glivec (imatinib)
Glivec® (imatinib) is approved in more than 110 countries for the treatment of all phases of Ph+ CML, for the treatment of adult patients with KIT (CD117)-positive gastrointestinal stromal tumors (GIST), which cannot be surgically removed and/or have metastasized and for the treatment of adult patients following complete surgical removal of KIT+ GIST. Take with food and a large glass of water.

Glivec Important Safety Information
Glivec can cause fetal harm in pregnant woman. Glivec has been associated with severe edema (swelling) and serious fluid retention. Cytopenias (anemia, neutropenia, thrombocytopenia) are common, generally reversible and usually managed by withholding Glivec or dose reduction. Monitor blood counts regularly. Severe congestive heart failure and left ventricle dysfunction, severe liver problems including cases of fatal liver failure and severe liver injury requiring liver transplants have been reported. Use caution in patients with cardiac dysfunction and hepatic dysfunction. Monitor carefully.

Bleeding may occur. Severe gastrointestinal (GI) bleeding has been reported in patients with KIT+ GIST. Skin reactions, hypothyroidism in patients taking levothyroxine replacement, GI perforation, in some cases fatal and tumor lysis syndrome, which can be life threatening, have also been reported with Glivec. Correct dehydration and high uric acid levels prior to treatment. Long-term use may result in potential liver, kidney, and/or heart toxicities; immune system suppression may also result from long-term use. In patients with hypereosinophilic syndrome and heart involvement, cases of heart disease have been associated with the initiation of Glivec therapy. Growth retardation has been reported in children taking Glivec. The long-term effects of extended treatment with Glivec on growth in children are unknown.

The most common side effects include fluid retention, muscle cramps or pain and bone pain, abdominal pain, loss of appetite, vomiting, diarrhea, decreased hemoglobin, abnormal bleeding, nausea, fatigue and rash.

Please see full Prescribing Information available at www.glivec.com.

Disclaimer
The foregoing release contains forward-looking statements that can be identified by terminology such as “to evaluate,” “can,” “potential,” “continued,” “dedication,” “ongoing,” “looking to the next phase and exploring,” “may,” continues,” “commitment,” “planned,” “will,” “aim,” “providing support,” or similar expressions, or by express or implied discussions regarding potential new indications or labeling for Tasigna or Glivec or regarding potential future revenues from such products . You should not place undue reliance on these statements. Such forward-looking statements reflect the current views of management regarding future events, and involve known and unknown risks, uncertainties and other factors that may cause actual results with Tasigna and Glivec to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that either Tasigna or Glivec will be approved for any additional indications or labeling in any market. Nor can there be

any guarantee that Tasigna or Glivec will achieve any particular levels of revenue in the future. In particular, management's expectations regarding Tasigna and Glivec could be affected by, among other things, unexpected regulatory actions or delays or government regulation generally; unexpected clinical trial results, including unexpected new clinical data and unexpected additional analysis of existing clinical data; the company's ability to obtain or maintain patent or other proprietary intellectual property protection; competition in general; government, industry and general public pricing pressures; unexpected manufacturing issues; the impact that the foregoing factors could have on the values attributed to the Novartis Group's assets and liabilities as recorded in the Group's consolidated balance sheet, and other risks and factors referred to in Novartis AG's current Form 20-F on file with the US Securities and Exchange Commission. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those anticipated, believed, estimated or expected. Novartis is providing the information in this press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

About Novartis
Novartis provides innovative healthcare solutions that address the evolving needs of patients and societies. Headquartered in Basel, Switzerland, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, eye care, cost-saving generic pharmaceuticals, preventive vaccines and diagnostic tools, over-the-counter and animal health products. Novartis is the only global company with leading positions in these areas. In 2012, the Group achieved net sales of USD 56.7 billion, while R&D throughout the Group amounted to approximately USD 9.3 billion (USD 9.1 billion excluding impairment and amortization charges). Novartis Group companies employ approximately 131,000 full-time-equivalent associates and operate in more than 140 countries around the world. For more information, please visit http://www.novartis.com.

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